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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/228,926	04/18/94	PAOLETTI	E 4543102430

EXAMINER	
MOSHER,M	
ART UNIT	**PAPER NUMBER**
1813	18

18N1/0712

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DATE MAILED: 07/12/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 3-16-95 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire Three (3) month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 33-51 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☒ Claims 33, 34, 40-43, 47-51 are rejected.

5. ☒ Claims 35-37, 39, 44-46 are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.

13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 2/93)

Applicant's request to designate claims 33-51 as corresponding the Count in interference 103,399, substitute the Count with claim 42 herewith, and redeclare the Interference with Paoletti as the Senior Party, is denied. Claims 33-48, 50 and 51 do not correspond to the pending interference count, because they do not contain the element of the promoter being "adjacent to" the foreign sequence, which is a key aspect of the count. Furthermore, claims 33-51 as currently written are not allowable, because applicant is not entitled to the full benefit of the filing dates claimed. This is discussed in detail below in the rejection of claims 33-51.

Exhibit A, a copy of a Disclosure Statement calling attention to the existence of interference 103,399, is noted. The original is not present in this application file. However, note has been taken of the interference.

Exhibits C and D, copies of motions made in the interference, are noted, but the intended purpose of these exhibits in this application are not clear.

Exhibits E and F, copies of declarations made in prosecuting European patents, are noted. It is not clear if these are intended to introduce facts into the record as equivalent to declarations under 35 USC §1.132; if this is the intent, the declarations are not in proper form.

Claims 48 and 49 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable

over claim 7 of U.S. Patent No. 4,603,112. Although the conflicting claims are not identical because they differ in scope, they are not patentably distinct from each other because the instant viruses are also claimed in the patent claim.

The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 40 is rejected under 35 U.S.C. § 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim. Plasmid pDP202 does not contain donor DNA not naturally occurring in vaccinia DNA, being merely the AvaI H fragment inserted into pBR322. See Figure 15B.

In making the rejections over prior art, applicants are denied the benefit of the filing dates of application serial numbers 06/334,456 (corresponding to U.S. patent 4,769,330; filing date December 24, 1981) and 06/446,824 (corresponding to U.S. patent 4,603,112; filing date December 8, 1982), for reasons discussed

immediately below. Therefore the effective filing date is seen as June 19, 1984.

In the '330 patent, there is no written description of what is now claimed, since there are no blazemarks to vaccinia promoters that exert functional control over the donor DNA. The passages of the '330 patent cited by applicant as supporting the claims have been considered.

In the '330 patent, column 8, line 64, through column 9, line 5 states:

> "The direction of inclusion... may be of importance in case promotion of transcription...is initiated by a promoter site within the F-fragment itself. However, HSV promoter sites do exist within the Bam HSV TK fragment itself, so that transcription of the HSV TK gene may occur no matter in which direction the Bam HSV TK fragment and HSV TK gene have been incorporated within the vaccinia HindIII F fragment".

This statement is equivocal in that it indicates two possibilities for expression control and does not indicate any preference regarding vaccinia expression control.

'330 column 10, lines 6-10, states:

> "Again, by in vivo processes within the cell, the mechanism of which are not known in detail, the HSV TK-modified fragment is incorporated into the vaccinia variants in the cell and is then capable of replication and expression under vaccinia

control".

This statement is equivocal in that it is not clear whether it means that replication occurs under vaccinia control and replication allows expression to occur, or that both replication and expression are under vaccinia control.

'330 column 28, lines 10-18, states in part:

"However, the variants VP-1, VP-3, and VP-5, derived from DP32, will not so express the gene, possibly because the orientation of the gene within the virus is contrary to the direction of gene transcription".

Clearly, "possibly" is an equivocation.

Considering the patent disclosure as a whole, in the light of the state of the art at the time the application was filed, there are no definite statements regarding expression under vaccinia control. Taken out of context, the passage from column 10 might be seen as a statement regarding vaccinia expression control; however, considering the amount of equivocation at the two passages which discuss expression control in more detail, the disclosure taken as a whole does not in any definite way teach or provide blazemarks to expression control by vaccinia promoters, as is now claimed. The equivocal speculative statements that expression "might be initiated by a promoter site within the vaccinia F fragment" and that "possibly...the orientation of the gene..is contrary to the direction of gene transcription" do not add up to blazemarks which

point the artisan in any definite sense to a promoter which exerts functional control over the donor DNA. Even, arguendo, should these passages be considered as providing "written description" support for what is now claimed, the disclosure does not provide any guidance as to how one would obtain additional vaccinia promoters, and thus as of December 24, 1981, enables only viruses which have the donor DNA inserted in the BamHI site of vaccinia virus fragment F.

The copy of the declarations by Paoletti (Exhibit E) and by Hruby (Exhibit F) in part address the interpretation of the teachings of the '330 patent by one skilled in the art, see pages 4-11 of Hruby and pages 8-14 of Paoletti. These declarations do not constitute declarations under 35 USC § 1.132, since there is no statement acknowledging that willful false statements and the like are punishable by law. In addition, even if the declarations met the formal requirements of § 1.132, they would not be convincing. It is noted that the portions of the declarations discussing the '330 patent teachings are the same for the two declarants, see sections 12-18 of Paoletti and 10-16 of Hruby. It is noted that Dr. Hruby is one who was highly skilled in the vaccinia virus art at the time the invention was made, and does not appear to be an interested party. The comments below therefore address the statements made by Dr. Hruby, although they apply with equal force to the same statements made by Dr. Paoletti. On page 6, lines 9-13,

Dr. Hruby states an expert opinion that the '330 patent "anticipated" certain subject matter, and the same subject matter was "certainly anticipated or suggested by the Panicali et al article either alone or in combination with other documents" (Panicali et al, Proceedings of the National Academy of Sciences USA, vol. 4927-4931, August 1982, reference BH in this application). The subject matter under discussion appears to be teachings in regard to vaccinia promoters controlling expression of foreign genes in recombinant viruses. The 1982 Panicali et al article was published after the filing of the application which matured into the '330 patent, and does not constitute material which was in the possession of those in the art at the time the invention of the '330 patent was made. However, the declaration discusses <u>together</u> the teachings of the Panicali article and the '330 patent. See pages 7-10, sections 11-17 of the Hruby declaration. While the teachings of the patent and the printed publication are largely similar, the 1982 Panicali et al article contains at least one statement providing a blazemark to a vaccinia promoter: on page 4391, "other (unpublished) data suggest that vaccinia signals may be operative for HSV TK expression". This statement regarding vaccinia signals is more definite than any statement made in the patent disclosure. Note in the declaration the difference between "anticipated", referring to the patent disclosure, and "certainly anticipated or suggested" referring to

the publication. This difference in phrasing suggests that the expert declarant considered the teachings of the publication to be different and greater than the teachings of the patent. It is submitted that, in the declarations, the teachings of the '330 patent are not discussed solely in the light of the state of the art as of the 1981 filing date, but also take into consideration the later teachings of the 1982 publication. Therefore it is concluded, in the absence of hindsight and considering the patent application as a whole in the absence of the teachings of the 1982 publication, the only statements made in the '330 patent disclosure are seen as equivocal and do not constitute blazemarks to the invention now claimed.

In the 4,603,112 patent, there are more definite blazemarks to two specific regions for insertion involving a vaccinia promoter. However, the description is limited to a "tentative site of promoter" near the BamHI site in HindIII F (supported by Figure 9A), and transcription regulatory signals upstream of central BamHI site in AvaI H (supported by Figure 15E and F and col. 25). However, there is no written description of the broadly claimed "expression under vaccinia control", nor guidance as to how to obtain additional control regions. Furthermore, while the disclosure, in one instance, "demonstrates conclusively that transcription in this recombinant virus is initiated by regulatory signals within the vaccinia genome" (emphasis added), there is no

broader teaching that regulatory signals within the vaccinia genome are not only sufficient for expression, but that these signals are also necessary for expression of a foreign gene. Therefore the written description and enablement as of the December 8, 1992 date are limited to the BamHI site in HindIII fragment F and the central BamHI site in AvaI fragment H, and do not support the full scope of what is now claimed.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 33, 34, 41, 42, 43, 50, and 51 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Mackett et al (Proc. Natl. Acad. Sci. USA vol. 79, p. 7415-7419, December 1982).

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of

> this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 38, 47, and 49 are rejected under 35 U.S.C. § 103 as being unpatentable over Mackett et al (Proc. Natl. Acad. Sci. USA vol. 79, p. 7415-7419, December 1982, reference AX) in view of Panicali et al (J. Virol. vol. 37, p. 1000-1010, 1981, reference BF). Mackett et al differs from these claims in that Mackett et al uses a 3kb AvaI/EcoRI fragment as the segment of vaccinia DNA rather than the AvaI H fragment. However, Mackett et al teaches that the AvaI/EcoRI fragment comes from a 9 kb segment of the vaccinia genome which is not essential for infectivity, and cites Panicali et al. Panicali et al teaches that the AvaI H fragment is in this 9 kb segment which is not essential for infectivity. Therefore use of the AvaI H fragment would have been an obvious variation upon use of the AvaI/EcoRI fragment taught by Mackett et al. The invention as a whole is therefore prima facie obvious, absent unexpected results.

Claim 40 is rejected under 35 U.S.C. § 103 as being

unpatentable over Panicali et al (J. Virol. vol. 37, p. 1000-1010, 1981, reference BF). Panicali et al teaches the isolated AvaI H fragment of the vaccinia virus genome and its use as probe distinguishing between L and S variants of vaccinia, see reference Figure 8. This differs from the claimed plasmid pDP202 only in that the AvaI H fragment is inserted into the vector pBR322 to make plasmid pDP202, see Figure 15B of the instant specification. It would have been within the ordinary skill of the art to clone the isolated AvaI H fragment into the standard vector pBR322, for easy preparation of the isolated DNA fragment for use as a probe. The invention as a whole is therefore prima facie obvious, absent unexpected results.

Claim 39 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form.

Claims 35-37 and 44-46 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy

as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph. D., whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday-Thursday from 6:30 AM-4:00 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christine Nucker, can be reached on (703) 308-4028.

The fax phone number for art unit 1813 is (703) 305-7939. Certain papers related to this application may be submitted by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (October 19, 1988) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

July 11, 1995

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800

JOHN J. DOLL
DIRECTOR
GROUP 1800